AMENDMENT

In the Specification:

Please insert a paper copy of the sequence listing as new pages 1 - 5 in the above-captioned patent application. A request to use a computer readable form from another application, in accordance with 37 C.F.R. §1.821(e), accompanies this response.

Please amend Table 1 on page 19 as follows:

Table 1
Primer pairs used for PCR amplification of rapamycin PKS cassettes.
All primers are listed from 5' to 3'.

Module	Primer	Sequence
rapAT2	forward:	TTTAGATCTGTGTTCGTCTTCCCGGGT (SEQ ID NO:1)
	reverse:	TTTCTGCAGCCAGTACCGCTGGTGCTGGAAGGCGTA (SEQ ID NO:2)
rapKR2	forward:	TTTCTGCAGGAGGGCACGGACCGGGCGACTGCGGGT (SEQ ID NO:3)
	reverse:	TTTTCTAGAACCGGCGGCAGCGGCCCGCCGAGCAAT (SEQ ID NO:4)
rapDH/KR4	forward:	TTCTGCAGAGCGTGGACCGGGCGGCT (SEQ ID NO:5)
	reverse:	TTTTCTAGAGTCACCGGTAGAGGCGGCCCT (SEQ ID NO:6)
rapDH/ER/KR1	forward:	TTTCTGCAGGGCGTGGACCGGGCGGCTGCC (SEQ ID NO:7)
(left half)	reverse:	TTTCTCGAGCACCACGCCCGCAGCCTCACC (SEQ ID NO:8)
rapDH/ER/KR1	forward:	TTTCTCGAGGTCGGTCCGGAGGTCCAGGAT (SEQ ID NO:9)
(right half)	reverse:	TTTTCTAGAATCACCGGTAGAAGCAGCCCG (SEQ ID NO:10)

Please amend the paragraph, beginning at page 19, line 13, as follows:

Replacement of DEBS Modules By Rapamycin PKS Cassettes

a) Replacement of DEBS DH/ER/KR4. A portion of the erythromycin gene of module 4 (eryDH/ER/KR4) was replaced either with the corresponding rapamycin activities of the first rapamycin module (rapDH/ER/KR1) or of module 4 of rapamycin (rapDH/KR4). The replacement utilized the technique of Kao *et al. Science* (1994) 265:509-512. A donor plasmid was prepared by first amplifying 1 kbp regions flanking the DH/ER/KR4 of DEBS to contain a PstI site at the 3' end of the left flank and an XbaI site at the 5' end of the right flank. The fragments were ligated into a temperature-sensitive donor plasmid, in a manner analogous to that set forth for KR6 in paragraph b) of this example. and the rapamycin cassettes prepared as described in Example 1 were inserted into the PstI/XbaI sites. The recipient plasmid was pCK7 described in Preparation A. The *in vivo* recombination technique resulted in the expression plasmid pKOS011-19 (eryDH/ER/KR4 → rapDH/ER/KR1) and pKOS011-21 (eryDH/ER/KR4 → rapDH/KR4). The junctions at which the PstI and XbaI sites were introduced into DEBS in both vectors are as follows (SEQ ID NOS:11-12):

GAGCCCCAGCGGTACTGGCTGCAG rap cassette TCTAGAGCGGTGCAGGCGGCCCCG

Please amend the paragraph, beginning at page 20, line 23, as follows:

Approximately 1 kb regions flanking the eryKR6 domain were PCR amplified with the following primers:

left flank	forward	5'-TTTGGATCCGTTTTCGTCTTCCCAGGTCAG	(SEQ ID NO:13)
	reverse	5'-TTTCTGCAGCCAGTACCGCTGGGGCTCGAA	(SEQ ID NO:14)
right flank	forward	5'-TTTTCTAGAGCGGTGCAGGCGGCCCCGGCG	(SEQ ID NO:15)
	reverse	5'-AAAATGCATCTATGAATTCCCTCCGCCCA	(SEQ ID NO:16)

Please amend the paragraph, beginning at page 20, line 26, as follows:

These fragments were then cloned into a pMAK705 derivative in which the multiple cloning site region was modified to accommodate the restriction sites of the fragments (i.e., BamHI/PstI for the left flank and XbaI/NsiI for the right flank). Cassettes were then inserted into the PstI/XbaI sites of the above plasmid to generate donor plasmids for the *in vivo* recombination protocol. The resulting PstI and XbaI junctions engineered into DEBS are as follows (SEQ ID NOS:17-18):

GAACACCAGCGCTTCTGGCTGCAG rap cassette TCTAGAGACCGGCTCGCCGGTCGG

Please amend the paragraph, beginning at page 21, line 21, as follows:

d) Replacement of DEBS AT2. The DEBS AT activity from module 2 was excised after inserting restriction sites BamHI and PstI flanking the AT module 2 domain into pCK12 (Kao *et al. J Am Chem Soc* (1995) 112:9105-9106). After digestion with BamHI/PstI, the BglII/PstI fragment containing rapAT2 was inserted. The resulting engineered DEBS/rapAT2 junction is as follows (BamHI/BglII ligation - GGATCT; PstI - CTGCAG) (SEE ID NOS:19-20):

AGTGCCTCCGACGGTGGATCT rapAT2 CTGCAGCCGGACCGCACCACCCCT

Please amend the paragraph, beginning at page 22, line 4, as follows:

A duplex oligonucleotide linker (ΔRdx) was designed to allow complete excision of reductive cycle domains. Two synthetic oligonucleotides (SEQ ID NOS:21-22):

5'-GCCGGACCGCACCACCCCTCGTGACGGAGAACCGGAGACGGAGAGCT-3'

3'-ACGTCGGCCTGGCGTGGTGGGGAGCACTGCCTCTTGGCCTCTGCCTCTCGAGATC-5'

were designed to generate PstI- and XbaI-compatible ends upon hybridization. This duplex linker was ligated into the PstI- and XbaI-sites of the recombination donor plasmid containing the appropriate left- and right-flanking regions of the reductive domain to be excised. The *in vivo* recombination technique of Example 2, paragraph a) was then used. The donor plasmid contained the duplex linker ΔRdx having a PstI and XbaI compatible end ligated into the PstI and XbaI sites of the plasmid modified to contain the left and right flanking regions of the reductive domain to be excised. The donor plasmids were recombined with recipient plasmid pCK7 to generate pKOS011-13 (eryKR6 → ΔRdx) and with recipient plasmid pCK13 to obtain pKOS005-4 (eryKR2 → ΔRdx). These plasmids generated, when transformed into *S. coelicolor* CH999, the polyketides 11-13 a,b,c and 5-4 a,b in Figure 5, respectively.

Please amend the paragraph, beginning at page 23, line 15, as follows:

The 1+2+TE PKS in pCK12 contained a fusion of the carboxy-terminal end of the acyl carrier protein of module 2 (ACP-2) to the carboxy-terminal end of the acyl carrier protein of module 6 (ACP-6). Thus ACP-2 is essentially intact and is followed by the amino acid sequence naturally found between ACP-6 and the TE. Plasmid pCK12 contained *ery*A DNA originating from pS1 (Tuan, J. S. *et al. Gene* (1990) 90:21). pCK12 is identical to pCK7 (Kao *et al. Science*

(1994), *supra*) except for a deletion between the carboxy-terminal ends of ACP-2 and ACP-6. The fusion occurs between residues L3455 of DEBS1 and Q2891 of DEBS3. An *Spe*I site is present between these two residues so that the DNA sequence at the fusion is CTCACTAGTCAG (SEQ ID NO:23).